REMARKS

The status of the claims is as follows:

Original:	None
Currently amended:	1
Previously presented:	None
Canceled:	2-47
New:	48-64

Claims 2-16, 26-35 and 37-47 are being canceled in this amendment. Claims 17-25 and 36 were canceled previously. Claims 48-64 are new. Claims 1 and 48-64 are pending with entry of this amendment.

Claim 1 has been amended to recite that the efavirenz is about 50% by weight of the total composition of the compressed tablet. Support for this amendment can be found in claim 1 as originally filed and in lines 11-12 on page 2 of the specification. The term "filler" in claim 1 has been replaced with "filler/disintegrant", which is the term originally used in claim 1. In addition, the term "diluent/compression aid" has been replaced with "filler/compression aid", which is the term that appears in the specification (see page 2, line 30 and page 3, line 3).

New claims 48-64 either correspond to or are similar to various of the canceled claims, and the new claims are fully supported by the application as originally filed in the same or similar manner as the canceled claims. None of the new claims introduces new matter.

Rejection under 35 U.S.C. § 103

Claims 1-15, 26-35 and 37-47 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Makooi in view of Remington. Claims 2-15, 26-35 and 37-47 have been canceled, rendering the rejection moot as applied thereto. This rejection is traversed with respect to claim 1 as amended herein and with respect to new claims 48-64.

For the reasons given in the response filed October 6, 2003 and incorporated by reference herein, it is Applicants' position that Makooi does not teach or suggest the use of a low level of superdisintegrant in efavirenz formulations, whether considered alone or in view of Remington. Quite the contrary, Makooi in view of Remington clearly directs the person of ordinary skill in the art to employ 10 wt.% or more of superdisintegrant.

The Examiner has admitted that Makooi does not teach a 1-5 wt.% superdisintegrant concentration, but has asserted that the distinction between the instant claims and Makooi is illusory in that the claimed tablets must contain both disintegrant and superdisintegrant and that

no distinction is drawn between disintegrants and superdisintegrants in the subject application. The Examiner has cited page 3, lines 21-27 of the application in support of his position.

As explained in the remarks included with the amendment filed March 18, 2004 and contrary to the Examiner's position, the subject application does draw a distinction between disintegrants and superdisintegrants. Lines 8-13 on page 3 provide a list of disintegrants. Lines 21-27 on page 3 subsequently state that certain of the disintegrants listed above at lines 8-13 are superdisintegrants; i.e., of the disintegrants listed at lines 8-13 the following are superdisintegrants: carboxymethylcellulose sodium, croscarmellose sodium, crospovidone, guar gum, polacrilin potassium, and pregelatinized starch. In other words, page 3 indicates that superdisintegrants represent a particular sub-class of disintegrants. Furthermore, the claims recite that the compressed tablet contains between about 1% and 5% by weight of a superdisintegrant. Whatever other components are present in the compressed tablet, whether those explicitly recited in the claim or those swept in by the transitional term "comprising", the tablet is restricted to about 1-5 wt.% of a superdisintegrant. Since Makooi teaches away from compositions containing about 1-5 wt.% of a superdisintegrant (i.e., as noted above, Makooi directs the skilled artisan to employ 10 wt.% or more of a superdisintegrant), the instant claims are neither taught nor suggested by Makooi. Remington merely provides a general description of tablet preparation and tablet ingredients. Remington does not disclose efavirenz, does not teach or suggest efavirenz-containing tablet compositions, and in no way contradicts Makooi's direction to the person of ordinary skill in the art to employ 10 wt.% or more of a superdisintegrant in efavirenz solid dosage forms. Accordingly, the claimed compressed tablet is not taught or suggested by Makooi in view of Remington, nor does the Makooi-Remington combination motivate the skilled artisan to make and use the claimed tablet. Instead Makooi + Remington direct the person of ordinary skill in the art toward compositions containing 10 wt.% or more of a superdisintegrant. Accordingly, Makooi in view of Remington does not render the claimed invention prima facie obvious, and withdrawal of the section 103 rejection is accordingly requested.

Declaration under 37 C.F.R. 1.132

Assuming strictly for the sake of argument that the claims were prima facie obvious, then the claims are patentable over Makooi + Remington in view of the unexpected results set forth in the Rule 132 Declaration of Munir Alwan Hussain (hereinafter the "Declaration") that accompanied the response filed October 6, 2003. The Declaration presents the results of several pharmacokinetic studies involving efavirenz tablets and capsules. These studies were bioequivalency studies that were part of the effort at DuPont Pharmaceutical Company (since acquired and now part of Bristol-Myers Squibb Pharma) to develop an efavirenz compressed tablet that was bioequivalent to the commercial capsule formulation of efavirenz. These studies demonstrated that tablets prepared in accordance with Makooi (i.e., tablets containing 50 or 60 wt.% efavirenz and 10 wt.% or more superdisintegrant) had less bioavailability than (and thus

were not bioequivalent to) efavirenz commercial capsules, whereas the tablets of the claimed invention (i.e., tablets containing 50 wt.% efavirenz and 4 or 5 wt.% superdisintegrant) had the same (i.e., were bioequivalent to) or better bioavailability than the capsules. This result is neither taught nor suggested by Makooi in view of Remington. Furthermore, per the Declaration, it is also noted that, absent the development of a tablet bioequivalent to the commercial capsule, a full scale clinical trial with a non-bioequivalent tablet is required to demonstrate the tablet's safety and efficacy. Conducting a full scale clinical trial is costly in terms of time and resources and can also substantially delay approval and launch. The claimed invention resulted in the development of an FDA-approved bioequivalent tablet without the need for a full scale clinical trial, a benefit not achieved via the Makooi invention. Clearly then, under the assumption that the claimed invention is prima facie obvious over the cited references (which it is not), the Declaration provides evidence of unexpected results rebutting the alleged prima facie case.

The Examiner has asserted that the Declaration is sufficient to overcome the rejection of claim 16 but is not commensurate in scope with the other claims. New claim 56 corresponds to claim 16, which has been canceled. Claim 56 recites a tablet composition containing specific ingredients in specific amounts, and corresponds to one of the tablet compositions used in the experiments described in the Declaration. The Examiner's interpretation of the results set forth in the Declaration is unreasonably narrow. It is Applicants' position that the evidence of unexpected results provided in the Declaration can be extrapolated to and is representative of the entire class of tablets embraced by the claims as amended herein. The Declaration shows that efavirenz tablets containing 50 wt.% efavirenz and 4 or 5 wt.% or less of superdisintegrant unexpectedly have better bioavailability than comparable tablets having 50 or 60 wt.% efavirenz and 10 wt.% or more superdisintegrant and unexpectedly have comparable or better bioavailability than commercial capsules. This showing supports the patentability of all of the claims in that each claim recites a tablet containing about 50 wt.% efavirenz and about 1-5 wt.% of a superdisintegrant.

The Examiner has asserted that Applicants have disregarded the general statement made in Makooi about the typical use of superdisintegrants in the art and has referred to col. 3, lines 35-40 which states that superdisintegrants are generally used in the art in amounts of 1-10 wt.% Applicants have not disregarded the Makooi statement and in fact addressed this statement in detail on page 2 of the response filed October 6, 2003. The statement in col. 3 is <u>not</u> an embodiment of the invention being claimed by Makooi, and in fact contrasts sharply with Makooi's teaching that very high levels of superdisintegrant are required for solid dosage forms containing efavirenz. Makooi explicitly notes this contrast at col. 4, lines 56-61. Thus, the person of ordinary skill in the art would understand that, while superdisintegrants are generally used at a low level in solid pharmaceutical dosage forms, low levels are <u>not</u> suitable for dosage forms containing efavirenz. Considered as a whole then, Makooi clearly suggests to the skilled artisan that a low level of superdisintegrant in efavirenz formulations is inappropriate. In view of

Makooi's teachings then, the use of superdisintegrants at concentrations below 10 wt.% in formulations containing efavirenz is an unexpected observation.

Claim Objection

Claim 16 has been objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form. New claim 56 corresponds to claim 16 which has been canceled. Accordingly, the claim objection is treated here as applying to claim 56. The Examiner's invitation to rewrite the claim in independent form is declined, because it is believed that the rejection of the base claim should be withdrawn for the reasons set forth above. Withdrawal of the objection is accordingly requested.

The application is believed to be in condition for allowance and passage to issue is requested. The Examiner is invited to telephone the undersigned should any minor matters need to be resolved before a Notice of Allowance can be mailed.

Respectfully submitted,

By 

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